|  |
| --- |
| **Table 1**. Characteristics of the study population (N=991) |
| **Characteristic** | **n** | **%** |
| **Sex** |  |  |
| Male | 487 | 49 |
| Female | 504 | 51 |
| **Country of residence\*** |  |  |
| Australia | 34 | 3 |
| Northern Europe  | 306 | 31 |
| Western Europe | 392 | 40 |
| Eastern Europe  | 74 | 8 |
| Southern Europe  | 42 | 4 |
| Western Asia | 143 | 14 |
| **Organ laterality** |  |  |
| Situs solitus  | 499 | 51 |
| Situs inversus | 348 | 35 |
| Heterotaxia | 13 | 1 |
| Situs status not reported | 131 | 13 |
| **Time period of birth** |  |  |
| Earlier than 1976 | 151 | 15 |
| 1977-1996 | 363 | 37 |
| 1997-2015 | 477 | 48 |
| **Diagnostic information** |  |  |
| Definite PCD diagnosis+  | 611 | 62 |
| Probable PCD diagnosis# | 207 | 21 |
| Clinical diagnosis only | 173 | 17 |
| **Age at diagnosis** |  |  |
| 0-9 years | 448 | 45 |
| 10-19 years | 317 | 32 |
| 20-29 years | 98 | 10 |
| 30-39 years | 61 | 6 |
| 40-49 years | 36 | 4 |
| ≥50 years | 31 | 3 |
| **BMI¶** |  |  |
| Underweight | 59 | 6 |
| Normal | 752 | 81 |
| Overweight | 116 | 13 |

\* Based on geographical region definitions of the United Nations Statistics Division (March 2017). Northern Europe: Denmark, Norway, United Kingdom; Western Europe: Belgium, France, Germany, Switzerland, the Netherlands; Eastern Europe: Poland; Southern Europe: Italy, Serbia; Western Asia: Cyprus, Israel, Turkey. + Defined as hallmark PCD electron microscopy findings and/or biallelic gene mutation identified based on the ERS PCD Diagnostics Guidelines [21]. # Abnormal light or high frequency video microscopy finding and/or low (≤ 77nl/min) nasal NO value. ¶BMI z-scores <=-1.96 underweight:, >-1.96 & <1.96 normal, >=1.96 overweight.

**Table 2.** FEV1 and FVC in patients with primary ciliary dyskinesia from the iPCD Cohort, compared to GLI 2012 references (N=991)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   |   | **FEV1** |  | **FVC** |
| **Characteristic** | **N** | **mean** **z-score** | **95% CI** | **p-value\*** | **N** | **mean** **z-score** | **95% CI** | **p-value\*** |
| **Total** | 991 | -1.52 | -1.62 | -1.41 |  | 981 | -0.77 | -0.88 | -0.66 |  |
| **Sex** |  |  |  |  | 0.03 |  |  |  |  | 0.20 |
| Male | 487 | -1.36 | -1.49 | -1.22 |  | 483 | -0.70 | -0.84 | -0.56 |  |
| Female | 504 | -1.57 | -1.70 | -1.43 |  | 498 | -0.83 | -0.97 | -0.69 |  |
| **Age group** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| 6-9 years | 271 | -0.84 | -1.03 | -0.65 |  | 272 | -0.31 | -0.51 | -0.11 |  |
| 10-13 years | 207 | -1.00 | -1.21 | -0.79 |  | 203 | -0.48 | -0.70 | -0.26 |  |
| 14-17 years | 191 | -1.51 | -1.73 | -1.29 |  | 186 | -0.84 | -1.07 | -0.61 |  |
| 18-21 years | 81 | -1.71 | -2.05 | -1.37 |  | 82 | -0.72 | -1.07 | -0.37 |  |
| 22-25 years | 55 | -1.70 | -2.12 | -1.29 |  | 53 | -0.73 | -1.17 | -0.29 |  |
| 26-29 years | 41 | -2.19 | -2.67 | -1.72 |  | 40 | -1.16 | -1.66 | -0.66 |  |
| 30-33 years | 28 | -3.14 | -3.71 | -2.56 |  | 28 | -1.91 | -2.51 | -1.31 |  |
| 34-37 years | 27 | -2.87 | -3.45 | -2.28 |  | 25 | -2.10 | -2.72 | -1.47 |  |
| 38-41 years | 17 | -2.72 | -3.45 | -1.98 |  | 17 | -1.51 | -2.27 | -0.75 |  |
| 42-45 years | 23 | -3.03 | -3.66 | -2.39 |  | 24 | -2.23 | -2.87 | -1.58 |  |
| 46-49 years | 15 | -2.87 | -3.66 | -2.08 |  | 16 | -2.02 | -2.81 | -1.24 |  |
| ≥50 years | 35 | -2.30 | -2.82 | -1.78 |  | 35 | -1.45 | -1.99 | -0.91 |  |
| **Country** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| Australia | 34 | -1.87 | -2.39 | -1.34 |  | 34 | -1.26 | -1.80 | -0.72 |  |
| Belgium | 69 | -1.11 | -1.49 | -0.74 |  | 69 | -0.03 | -0.42 | 0.36 |  |
| Cyprus | 27 | -1.84 | -2.43 | -1.25 |  | 27 | -1.81 | -2.42 | -1.20 |  |
| Denmark | 74 | -1.19 | -1.55 | -0.82 |  | 74 | -0.58 | -0.95 | -0.20 |  |
| France | 75 | -1.30 | -1.66 | -0.94 |  | 72 | -0.36 | -0.74 | 0.02 |  |
| Germany | 142 | -1.36 | -1.62 | -1.10 |  | 137 | -0.79 | -1.06 | -0.52 |  |
| Israel | 87 | -1.53 | -1.86 | -1.20 |  | 84 | -1.08 | -1.43 | -0.74 |  |
| Italy | 35 | -1.29 | -1.81 | -0.78 |  | 35 | -0.35 | -0.89 | 0.18 |  |
| Netherlands | 66 | -0.39 | -0.77 | -0.02 |  | 66 | 0.74 | 0.35 | 1.13 |  |
| Norway | 14 | -1.42 | -2.23 | -0.61 |  | 14 | -1.00 | -1.83 | -0.16 |  |
| Poland | 74 | -1.84 | -2.20 | -1.48 |  | 74 | -0.91 | -1.28 | -0.54 |  |
| Serbia | 7 | -2.22 | -3.36 | -1.07 |  | 7 | -2.38 | -3.56 | -1.19 |  |
| Switzerland | 40 | -1.69 | -2.17 | -1.20 |  | 40 | -1.05 | -1.55 | -0.55 |  |
| Turkey | 29 | -1.72 | -2.30 | -1.14 |  | 29 | -1.50 | -2.10 | -0.90 |  |
| UK | 218 | -1.78 | -2.00 | -1.57 |  | 219 | -1.11 | -1.33 | -0.89 |  |
| **Diagnostic certainty** |  |  |  |  | 0.52 |  |  |  |  | 0.23 |
| Definite PCD diagnosis+ | 611 | -1.47 | -1.59 | -1.34 |  | 608 | -0.74 | -0.87 | -0.60 |  |
| Probable PCD diagnosis# | 207 | -1.55 | -1.76 | -1.33 |  | 203 | -0.94 | -1.16 | -0.71 |  |
| Clinical diagnosis only | 173 | -1.36 | -1.60 | -1.11 |   | 170 | -0.67 | -0.93 | -0.41 |   |

Mean z-scores (95%CI) for each group after adjusting for the remaining characteristics. \* likelihood ratio test p-value indicating whether the characteristic explains differences in FEV1 within the study population. + defined as hallmark PCD electron microscopy findings and/or biallelic gene mutation identified based on the ERS PCD Diagnostics Guidelines [25].

# abnormal light or high frequency video microscopy finding and/or low nasal NO value

**Table 3.** FEV1 and FVC of PCD patients of the iPCD Cohort with available ultrastructural defect information compared to GLI 2012 references

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **FEV1** |  | **FVC** |
| **Characteristic** | **N** | **mean****z-score** | **95% CI** | **p-value**¶ | **N** | **mean****z-score** | **95% CI** | **p-value**¶ |
| **Total** | 689 | -1.52 | -1.65 | -1.40 |  | 683 | -0.79 | -0.92 | -0.66 |  |
| **Sex** |  |  |  |  | 0.25 |  |  |  |  | 0.52 |
| Male | 344 | -1.46 | -1.62 | -1.29 |  | 341 | -0.76 | -0.93 | -0.58 |  |
| Female | 345 | -1.59 | -1.75 | -1.43 |  | 342 | -0.83 | -1.00 | -0.66 |  |
| **Age group** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| 6-9 years | 127 | -0.77 | -1.04 | -0.49 |  | 126 | -0.25 | -0.54 | 0.03 |  |
| 10-13 years | 148 | -1.19 | -1.44 | -0.94 |  | 147 | -0.65 | -0.91 | -0.39 |  |
| 14-17 years | 152 | -1.51 | -1.76 | -1.26 |  | 151 | -0.84 | -1.10 | -0.58 |  |
| 18-21 years | 69 | -1.53 | -1.89 | -1.17 |  | 68 | -0.62 | -1.00 | -0.23 |  |
| 22-25 years | 51 | -1.66 | -2.09 | -1.23 |  | 50 | -0.61 | -1.05 | -0.16 |  |
| 26-29 years | 35 | -2.14 | -2.66 | -1.63 |  | 34 | -1.17 | -1.71 | -0.63 |  |
| 30-33 years | 23 | -2.47 | -3.10 | -1.84 |  | 22 | -1.42 | -2.09 | -0.76 |  |
| 34-37 years | 20 | -2.67 | -3.34 | -1.99 |  | 21 | -1.74 | -2.43 | -1.06 |  |
| 38-41 years | 10 | -2.37 | -3.33 | -1.41 |  | 10 | -1.00 | -2.00 | -0.01 |  |
| 42-45 years | 10 | -3.24 | -4.20 | -2.28 |  | 11 | -2.86 | -3.81 | -1.91 |  |
| 46-49 years | 17 | -3.00 | -3.74 | -2.25 |  | 16 | -2.05 | -2.84 | -1.25 |  |
| ≥50 years | 27 | -2.34 | -2.93 | -1.75 |  | 27 | -1.29 | -1.90 | -0.68 |  |
| **Country** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| Australia | 31 | -1.82 | -2.36 | -1.28 |  | 31 | -1.18 | -1.74 | -0.62 |  |
| Belgium | 66 | -1.20 | -1.59 | -0.82 |  | 66 | 0.03 | -0.36 | 0.43 |  |
| Cyprus | 27 | -2.02 | -2.62 | -1.43 |  | 27 | -1.79 | -2.40 | -1.17 |  |
| Denmark | 23 | -1.36 | -1.99 | -0.72 |  | 23 | -0.60 | -1.26 | 0.05 |  |
| France | 59 | -1.28 | -1.68 | -0.87 |  | 59 | -0.45 | -0.87 | -0.03 |  |
| Germany | 83 | -1.21 | -1.54 | -0.87 |  | 79 | -0.69 | -1.05 | -0.33 |  |
| Israel | 67 | -1.46 | -1.83 | -1.08 |  | 64 | -0.89 | -1.28 | -0.49 |  |
| Italy | 35 | -1.46 | -1.98 | -0.95 |  | 35 | -0.65 | -1.19 | -0.12 |  |
| Netherlands | 30 | -0.45 | -1.01 | 0.11 |  | 30 | 0.66 | 0.08 | 1.24 |  |
| Norway | 13 | -1.43 | -2.27 | -0.60 |  | 13 | -0.84 | -1.71 | 0.03 |  |
| Poland | 39 | -1.80 | -2.30 | -1.30 |  | 39 | -0.89 | -1.41 | -0.37 |  |
| Serbia | 2 | -1.77 | -3.97 | 0.44 |  | 2 | -2.39 | -4.68 | -0.11 |  |
| Switzerland | 24 | -1.45 | -2.10 | -0.81 |  | 24 | -0.83 | -1.50 | -0.16 |  |
| Turkey | 7 | -2.12 | -3.28 | -0.96 |  | 7 | -2.13 | -3.33 | -0.92 |  |
| UK | 183 | -1.90 | -2.13 | -1.67 |  | 184 | -1.19 | -1.43 | -0.96 |  |
| **Ultrastructural defect\*** |  |  |  |  | 0.01 |  |  |  |  | 0.18 |
| Non-diagnostic | 123 | -1.19 | -1.48 | -0.91 |  | 120 | -0.74 | -1.04 | -0.44 |  |
| Dynein arm defects | 425 | -1.50 | -1.65 | -1.35 |  | 422 | -0.73 | -0.88 | -0.57 |  |
| Microtubular defects  | 134 | -1.91 | -2.20 | -1.63 |  | 134 | -1.08 | -1.37 | -0.78 |  |
| Acilia | 7 | -1.44 | -2.64 | -0.24 |   | 7 | -0.40 | -1.64 | 0.85 |   |

Mean z-scores (95%CI) for each group after adjusting for the remaining characteristics

¶ Likelihood ratio test p-value indicating whether the characteristic explains differences in FEV1 or FVC within the study population

+ Defined as hallmark PCD electron microscopy findings and/or biallelic gene mutation identified based on the ERS PCD Diagnostics Task Force guidelines [26]

# Abnormal light or high frequency video microscopy finding and/or low nasal NO value

\* Dynein arm defects: Outer and/or inner dynein arm defects, Microtubular defects: central pair, tubulus disorganisation, tubular transposition and/or nexin link defect.



**Fig 1.** FEV1 and FVC in PCD patients by age group compared to GLI 2012 reference values. FEV1 and FVC are presented as mean z-score (95%CI) after adjusting for sex, country, and level of diagnostic certainty. The dashed line shows the mean z-score of the normal population.

****

**Fig 2.** FEV1 and FVC in PCD patients by country compared to GLI 2012 reference values. FEV1 and FVC are presented as mean z-score (95%CI) after adjusting for sex, age group, and level of diagnostic certainty. The dashed line shows the mean z-score of the normal population.

****

**Fig 3.** FEV1 and FVC in PCD patients by sex, situs anomalies, and BMI compared to GLI 2012 reference values. FEV1 and FVC are presented as mean z-score (95%CI) after adjusting for age, country, and level of diagnostic certainty. The dashed line shows the mean z-score of the normal population.

****

**Fig 4.** Associationof FEV1 and FVC of PCD patients with CF patients. FEV1 and FVC are presented as mean %predicted (95% CI), without adjusting for other factors. The dashed line shows the mean of the normal population.